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Applicants: Thomas P. Abbott et al.

Application No.: 10/633,252

Filed: August 1, 2003

Title: 3-Methoxybenzyl Thiourea Derivatives and Improved Lipid Compositions Containing Same

Group Art Unit: 1621

Examiner: Elvis O. Price

Certificate of Mailing

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September 16, 2005 Roberta L. Hastreiter
Date Registration No. 32,990
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SECOND DECLARATION OF THOMAS P. ABBOTT FILED UNDER 37 C.F.R. §1.132

THOMAS P. ABBOTT declares as follows:

1. I received a B.S. is chemistry at the University of Akron in Akron, Ohio, in 1964. Completing a thesis entitled, "Complexes of Styrene with Maleic Anhydride, Fumaronitrile and Methyl Methacrylate," I received a M.S. in polymer chemistry at the University of Akron in 1968. Completing a thesis entitled, "Reactivity of Methyl Methacrylate Units in Copolymers," I received a Ph.D. in polymer chemistry at the University of Akron, Institute of Polymer Science, in 1972.

2. From 1964 to 1969, I was a research chemist for Gencorp Corporate Research in Akron, Ohio, and was responsible for the identification and analysis of in-house research and production problems and competitive products. From 1971 to 1995, I was a research chemist for the National Center for Agricultural Utilization Research, United States Department of Agriculture, in Peoria, Illinois, and performed research on natural products (lignin, starch, gums, protein, bioactive plant components, etc.) to develop new products and unique processes. From 1995 to 2001, I was a research leader in the New Crops and Processing Research Unit of the National Center for Agricultural Utilization Research, United States Department of Agriculture, in Peoria, Illinois, and directed ten Ph.D. researchers and twenty-six staff members in agricultural products and processing research, and in natural products research, under a budget of 2.6 million dollars. I am currently the sole proprietor of a company named "Value-added Products from Nature," which is registered in the state of Washington.

3. I was a member of the American Oil Chemists Society from 1993 to 2001, and was a board member of the IOP division of this society in 1999. I was also a member of the American Chemical Society from 1971 to 2000, the president of the Association for the Advancement for Industrial Crops from 1996 to 1997, and the president of the American Kenaf Society in 2000. I am currently a member of the Association for the Advancement of Industrial Crops, and of the American Kenaf Society.

4. During my professional career, I have been an author of, or a named inventor on, more than one hundred publications or patents, respectively, including the following publications discussing antioxidants:

(a) Isbell, T.A., Abbott, T.P., and Carlson, K.D., "Oxidative Stability Index of Vegetable Oils in Binary Mixtures with Meadowfoam Oil," Ind. Crops Prod 9, 115-123 (1999);

(b) Abbott, T.P., Wohlman, A., and Momany, F.A., "Antioxidant from Meadowfoam Stabilizes other Oils," Abstracts of the 2000 AAIC Meeting, October 15-17, 2000, St. Louis, MO, Page 28; and

(c) Abbott, T.P., Wohlman, A., Isbell, T.A., Momany, F.A., Cantrell, C., Garlock, D.V., and Weisleder, D., "1,3-di(3-Methoxybenzyl) Thiourea and Related Lipid Antioxidants," Ind. Crops. Prod. 16:43-58 (2002).

5. I am a natural products chemist specializing in natural polymers. My profession is supported by my degree in polymer science (chemistry), numerous publications that I have authored or co-authored regarding proteins, carbohydrate polymers, lignin, gums and other natural polymers, as well as my five years of employment at Gencorp Central Research analyzing and identifying polymer formulations.

6. I have extensive knowledge about chemistry, and about thiourea compounds.

7. I am one of the two inventors of the invention described in the above-identified continuation application ("the application"), along with Alan Wohlman (hereinafter "the inventors").

8. I am informed that, in an official action dated May 18, 2005 for the application ("the office action"), the examiner at the U.S. Patent and Trademark Office rejected claims 1, 2, 5, 37 and 39 of the application under 35 U.S.C. §101 as claiming the same invention as that of claims 7 and 8 of U.S. Patent No. 6,586,628 ("the '628 patent").

9. I have reviewed the '628 patent in its entirety.

10. It is my opinion as an expert in the area of thiourea compounds that, for the reasons set forth below, the subject matter that is described in claims 7 and 8 of the '628 patent would not have suggested that the invention that is described in claims 1, 2, 5, 37

and 39 of the application (as these claims have been amended in an accompanying amendment and response to the office action) would have a reasonable likelihood of success.

11. A significant amount of unpredictability exists in the art of disubstituted thiourea compounds, to which claims 1, 2, 5, 37 and 39 of the application are directed. In a Declaration of Thomas P. Abbott under 37 C.F.R. §1.132 dated July 3, 2003 (submitted to the U.S. Patent and Trademark Office for the application on August 1, 2003), which is incorporated by reference herein in its entirety, I discuss the fact that thiourea compounds that may appear to have similar chemical structures may have very different chemical properties (i.e., that unpredictability exists in this area). For example, I state (pages 4-7) that it is my opinion as an expert in the area of thiourea compounds that, for the reasons that I present in the declaration, 1,3-di(4-methoxybenzyl)thiourea has a different chemical structure, and different chemical properties, in comparison with 1,3-di(3-methoxybenzyl) thiourea, and that the structural difference between these two compounds results in these compounds having different chemical properties. Most significant in connection with the application is that, in comparison with 1,3-di(3-methoxybenzyl) thiourea, 1,3-di(4-methoxybenzyl)thiourea is significantly less soluble in lipids and oils and, as a result, has a significantly decreased ability to enhance the oxidative stability of a lipid or oil to which the compound is added. The less soluble a substituted thiourea compound is in a lipid or oil to which the compound is added, the less the compound will have the ability to enhance the oxidative stability of the lipid or oil (because more of it remains in an undissolved state). These statements are supported by experiments that are described in that Declaration.

The compounds that are described in claims 1, 2, 5, 37 and 39 of the application, as they have been amended, are thiourea compounds that have a different molecular structure and chain length from the 1-(3-methoxybenzyl)-3-octadecyl thiourea and 1-(3-methoxybenzyl)-3-octyl thiourea compounds that are described in claims 7 and 8 of the '628 patent, respectively.

As a polymer chemist, I am aware of a number of systems in which small differences in chain length of additives produce dramatic differences in compatibility

with a polymer system. For example, in the case of polyvinyl chloride, dioctyl phthalate is unusually compatible with the polymer, making it the preferred and most efficacious plasticizer used. Chain lengths that are shorter or longer are much less efficacious because their compatibility is limited, which causes these structures to exude out of the polymer. The same is true in the case of erucamide used as an antiblocking agent in extruded polymers. Amides of slightly higher and lower chain length are less effective and have dramatically different properties in this application.

Dispersability and water, polymer and/or solvent solubility change dramatically and unpredictably with sidechain length for many different structures and applications, including disubstituted thioureas. Thus, it is generally true that in polymer systems, or in lipids and/or oils, additives may have dramatically different effects with even small changes of one or two carbons in sidechain length, and that these effects are often surprising and unexpected. For example, a disubstituted thiourea that has a low solubility in lipids and oils may, as is discussed above, have a significantly decreased ability to enhance the oxidative stability of a lipid or oil to which the compound is added.

In conceivable applications of thiourea antioxidants, the effects of chain length would need to be determined. In some packaging coatings, an antioxidant is added to the coating to prevent rancidity in an enclosed food. In these cases, solubility in the polymer coating, and lack of extractability into the fats and oils of the food, are important for efficacy. Partitioning and compatibility are not predictable and would be expected to be optimum for one sidechain length over others adjacent to it. In the application of metal can linings made from crosslinked castor oil, it is unpredictable which antioxidants would be most compatible with the polymer can coating and least extractable into aqueous food systems, but it would be expected that a thiourea with a different sidechain length than in the packing coating would be optimum and that one antioxidant would differ from its similar homologues. In some cases of lipid systems for exterior body applications, either a thiourea structure insoluble in the biological system might be needed as in a protective barrier coating or a cell wall penetrating structure might be needed as in therapeutic topical applications. In both cases, only one structure of specific sidechain length would be expected to meet the desired properties optimally and be compatible with the formulation.

12. I am also informed that, in the official action, the examiner rejected claims 11-14 and 18-32 of the application under 35 U.S.C. §101 as claiming the same invention as that of claims 16-19 of U.S. Patent No. 6,545,052 ("the '052 patent").

I am further informed that, in the official action, the examiner rejected claims 1, 4, 7-11, 15-17, 33-36, 40 and 41 of the application under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-21 of the '052 patent.

13. I have reviewed the '052 patent in its entirety.

14. It is my opinion as an expert in the area of thiourea compounds that, for the reasons that have already been set forth hereinabove, and for the additional reasons set forth below, the subject matter that is described in claims 1-21 of the '052 patent would not have suggested that the invention that is described in any of claims 1, 4, 7-36, 40 and 41 of the application (as these claims have been amended in an accompanying amendment and response to the office action) would have a reasonable likelihood of success.

15. As is discussed hereinabove, a significant amount of unpredictability exists in the art of disubstituted thiourea compounds, to which claims 1, 4, 7-36, 40 and 41 of the application are directed (disubstituted thiourea compounds, compositions containing these compounds and methods of using these compounds).

16. Claims 1-21 of the '052 patent each describe an inhibition of free radical degradation of skin or hair of a human or nonhuman animal. In contrast, claims 1, 4, 7-36, 40 and 41 of the application (as they have been amended in the accompanying amendment and response) each describe an enhancement of an oxidative stability of a lipid or oil to which a disubstituted thiourea compound has been added.

It is clear from a review of claims 1-21 of the '052 patent and claims 1, 4, 7-36, 40 and 41 of the application that the problems that the inventors of the invention described in the '052 patent were attempting to solve are completely different from the

problem with which the inventors of the invention described in the rejected claims of the present patent application were concerned.

The chemical mechanisms for inhibiting free radical degradation of the skin or hair of a human or nonhuman animal and related properties are substantially different from the chemical mechanisms for enhancing an oxidative stability of a lipid or oil to which a disubstituted thiourea compound has been added.

In the case of oxidative stability enhancement of unsaturated oils, there are many mechanisms by which oxidative stability may be enhanced, but thioureas are known to be decomposers of hydroperoxy derivatives of the oils, which are the first product of reaction between oxygen and the oil. The subsequent degradation of the oil by cleavage to low molecular weight aldehydes and acids is, thus, avoided and oxidative stability is enhanced. (See page 70 of the enclosed article (pages 67-77) entitled "Impact of High-Temperature Food Processing on Fats and Oils," by Kathleen Warner, which is an excerpt from Impact of Processing on Food Safety, L. S. Jackson and J.N. Morgan, Eds, Proceedings of the American Chemical Society Symposium on Impact of Processing on Food Safety, Kluwer Academic/Plenum Publishers, New York, 1999. ISBN 0-306-46051-3).

In the case of free radical inhibition, the double-bonded sulfur in the thiourea compound is capable of absorbing additional free radicals and reacting with free radicals to form new compounds that are incapable of skin or hair damage. In the case of singlet oxygen free radicals, a high energy free radical, which can form from oxygen and sunlight, the sulfur molecule readily donates an electron to form a bond from the free radical, which changes it into a low energy species having no cell destructive attributes. In the same way, it was demonstrated experimentally in example 10 of the '052 patent that the 1,3-di(3-methoxybenzyl)thiourea compound described therein inhibits high energy free radicals which were capable of initiating free radical polymerization of acrylic acid. It does so by direct reaction of the thiourea sulfur with the free radicals to form more stable structures which are not capable of initiating polymerization. The free radical inhibition demonstrated in example 10 could not have been by the degradation of hydroperoxides because hydroperoxides are not formed in the AIBN chemically generated free radical initiation of polymerization of acrylic acid.

It is difficult to differentiate free radical inhibition and lipid hydroperoxide decomposition in lipid systems. In one publication concerning ester lubricants (copy enclosed), which is entitled "Some Synergistic Antioxidants for Synthetic Lubricants" (T. S. Chao et al., Proceedings of the Symposium on Synthetic Lubricants, American Chemical Society, 362-379 (1982)), an aromatic amine, N-phenyl-alpha-napphthlamine (PANA), as a free radical trapping agent, was combined with diphenyl thiourea. The authors conclude in this publication (page 365):

> "For the synergistic antioxidants covered in this paper, we believe the sulfur compounds act as peroxide decomposers and the synergism is caused by the presence of both the peroxide decomposer and the aromatic amine free radical traps. . ."

Furthermore, on pages 214-216 of the chapter entitled "Thiones" (compounds containing C=S bonds) of the book Atsuyoshi Ohno, Organic Chemistry of Sulfur (Plenum Press, New York, 1977), S. Oae describes the free radical trapping mechanism of thiones, which includes thioureas (copy enclosed). In contrast, in the book Autooxidation of Hydrocarbons and Polyolefins. Kinetics and Mechanisms," by Leo Reich et al. (Marcel Dekker, Inc. New York, 1969), on pages 141-145 of the Chapter entitled "Modes of Antioxidant Action" (copy enclosed), sulfur-containing antioxidants are shown to decompose hydrocarbon hydroperoxides without a free radical mechanism.

Additionally, the Oxidative Stability Index (OSI) test that is described in the present application (page 8 and examples), which was carried out at a temperature ranging from 110-130°C, is a destructive test. It is well known by experts in the field that the mechanism of oxidative decomposition of triglycerides at a temperature ranging from 110-130°C is different from the mechanism of free-radical damage to skin or hair. Specifically, the OSI test used in the application is an accelerated aging test intended to determine the antioxidative effect of additives on the decomposition of triglycerides. In this test, air is passed through heated oil until the oil decomposes to small molecules, such as acetic and butyric acids, which are low molecular weight breakdown products of triglycerides, and which are carried over in an air purge into a water solution, where conductivity measures a rapid increase in these small molecules in water.

From the above analysis, it can be concluded that an OSI test performed at a temperature ranging from 110-130°C with bulk oil, and activated by oxygen in continuously purging air, to measure low molecular weight breakdown products of triglycerides, is not a predictor of free radical inhibition of polymer crosslinking of protein (skin or hair) in an aqueous media at a lower temperature. Free-radical formation and skin or hair (protein) deterioration are different from the antioxidant effects observed at 110-130°C.

Moreover, I have enclosed an article entitled, "Review, The Problems of Using One-Dimensional Methods to Evaluate Multifunctional Food and Biological Antioxidants" (Edwin N. Frankel et al., Journal of the Science of Food and Agriculture 80, 1925-1941, 2000), the authors of which are leading world experts in antioxidants. In this article, the authors describe the unpredictable nature of antioxidant activity and a variety of factors that influence antioxidant activity, including the type of substrate and the temperature of the testing conditions. The authors show that the effectiveness of antioxidants is strongly dependent on the test system, the physical states of the lipid substrates, the conditions of oxidation, the oxidizing substrate, the localisation of antioxidants and the method employed to evaluate oxidation and the stages of oxidation.

In this paper, the authors also demonstrate that the difference between the testing of a bulk oil medium at a high temperature (as is described in the patent application) and a free radical inhibitor present in aqueous media (as is described in the '052 patent) leads to different results, and to different applications, for antioxidants. On pages 1928-1930 of this article, the authors describe the reversal of ranking or elimination of antioxidant activity when tests are conducted in aqueous emulsions as compared to activity in bulk oils.

Regarding the above issues, this article makes the following statements at the locations indicated:

Abstract

"The activity of antioxidants in foods and biological systems is dependent on a multitude of factors, including the colloidal properties of the substrates, the conditions and stages of oxidation and the localisation of antioxidants in different phases. When testing natural antioxidants in

vitro, it is therefore important to consider the system composition, the type of oxidisable substrate, the mode of accelerating oxidation, the methods to assess oxidation and how to quantify antioxidant activity. Antioxidant effectiveness is also determined by the heterogeneity and heterophasic nature of the system, the type of lipid substrate, including its physiochemical state and degree of unsaturation, the types of initiators, notably transition metals, other components and their possible interactions. For this reason, there cannot be a short-cut approach to determining antioxidant activity. Each evaluation should be carried out under various conditions of oxidation, using several methods to measure different products of oxidation. . . Several recent studies on natural phytochemical compounds produced conflicting results because non-specific and one-dimensional methods were used to evaluate antioxidant activity. There is a great need to standardise antioxidant testing to minimize the present chaos in the methodologies used to evaluate antioxidants. . ."

Page 1925

". . . Although there is a great multiplicity of methods used for antioxidant testing, there are no approved, standardised methods. Several rapid test methods to screen for antioxidant activity have been published and many different in vitro antioxidant protocols are currently used to evaluate antioxidants of interest in food and nutrition, health and disease. Obviously, the significance and relevance of antioxidant evaluations for food and biological systems depend strongly on the test method. Inconsistent results have been obtained for a number of recognised antioxidants depending on the methods used to test activity."

Pages 1926-1927

". . . Misleading data can be obtained in many of these test systems by neglecting important compositional and interfacial phenomena concerning charge and solubility of multiple components in real food or biological systems that strongly affect antioxidant performance.

. . . The effectiveness of antioxidants in complex heterogeneous foods and biological systems and in multiphase models is affected by many factors. Notable factors include the partitioning properties of the antioxidants between lipid and aqueous phases, the oxidation conditions and the physical state of the oxidisable substrate. Clearly, the influence of all relevant parameters cannot be evaluated by using only a one-dimensional assay protocol. Of particular importance are the conditions used to accelerate oxidation by raising the temperature, by using transition metal catalysts or other types of initiators, by increasing surface and by exposing to light of varying intensity."

Page 1928

"Antioxidant action becomes more complex in real foods and biological systems where a variety of mechanisms become effective, including free radical chain breaking, oxygen scavenging, singlet oxygen quenching, metal chelation and inhibition of oxidative enzymes. . . Meaningful interpretation of antioxidant action requires specifying the oxidising substrate protected by the putative antioxidant. . . .

. . . The activity of different types of antioxidants can vary significantly depending on whether the lipids are triacylglycerols, methyl esters, free fatty acids or incorporated into various biological particles such as lipoproteins or liver microsomes. Whether the antioxidants function in aqueous, bulk lipid or in heterophasic systems is critically important."

Page 1929

". . . The phenomenological observation that polar antioxidants are more active in bulk oil systems whereas non-polar antioxidants are more active in lipid suspended in aqueous systems was referred to as the 'polar paradox' by Porter. . . This interfacial phenomenon was explained by differences in the affinity of hydrophilic and lipophilic antioxidants towards the air, oil and water phases as well as the interface. . ."

Pages 1929-1930

". . . The partitioning properties of a particular antioxidant not only depend on the chemical structure and relative polarity of the antioxidant, but also vary according to the lipid substrates, surfactants, pH, temperature and the composition of the phases. . .

In summary, antioxidant effectiveness in multiphase food and biological systems is affected by important factors determined by interfacial phenomena governing the localisation and orientation of antioxidants by partitioning between the aqueous phase and the lipophilic phase and by interacting with the emulsifier at the interface. . . More knowledge is required on the partitioning behavior and efficiency of antioxidants in different phases to improve our understanding of antioxidant properties in different colloidal food and biological systems.

. . . The relative activity of various antioxidants depends on the type of substrate (eg phospholipid vs triacylglycerols and free fatty acids), the degree of lipid unsaturation and the physiochemical state of the oxidizable substrate. Some of the observed differences are attributable to the degree of heterogeneity of the system as discussed above, and complicated by the colloidal properties of the lipid substrate. . .

. . . In contrast to triacylglycerols, linoleic acid forms micelles in aqueous systems, which have different colloidal properties strongly affecting the behavior of both oxidation initiators and antioxidants."

Pages 1931-1932

"Many examples in the literature show that phenolic compounds can have either antioxidant activity or prooxidant activity depending on the oxidizing target and conditions used in the test system. A number of examples illustrate the variation in activity of antioxidants tested in different lipid systems (Table 3). Hydrophilic polyphenolic compounds showed significantly different trends in antioxidant activity when tested in three different systems. . .

The antioxidant effectiveness of rosemary extracts, carnosol and carnosic acid, was significantly influenced by the type of system tested, the oil substrates, the methods used to follow oxidation, and the concentrations of test compounds. Although the rosemary extracts and compounds effectively inhibited oxidation in corn oil, soybean oil, peanut oil and fish oil, when tested in bulk, these compounds were either inactive or promoted oxidation in the corresponding vegetable oil-in-water emulsion. . .

In conclusion, the structure-activity relationship of natural phenolic antioxidants is not only significantly affected by the test system used and the biological targets to be protected, but also by the modes of inducing oxidation and by the method used to determine oxidation.* Antioxidant activity may be further modulated by other components present in the test system."

*This statement would apply to all antioxidants, not just to phenolics.

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". . . These data emphasize that the ranking of antioxidant activity is strongly dependent on the test system and on the substrate to be protected by the antioxidants. . .

RECOMMENDED PROTOCOLS

We have seen in this survey that the effectiveness of antioxidants is strongly dependent on the test system, the physical states of the lipid substrates, the conditions of oxidation, the oxidizing substrate, the localisation of antioxidants and the method employed to evaluate oxidation and the stages of oxidation. . .

. . . Various testing protocols should consider the following parameters. . .

(1) Substrates. Use substrates relevant to foods and biological systems. . . Free fatty acids should be avoided because they form miscelles in which antioxidants behave differently than in triacylglycerols.

(2) Conditions. Test under various conditions, including different temperatures (below 60°C), metal catalysts and surface exposures. Select conditions to simulate real food or biological systems as closely as possible, depending upon the application. . .

In biological systems, phenolic compounds can participate in several antioxidant defences, including preventing oxidant formation, scavenging activated oxidants, reducing active intermediates and inducing repair systems. To improve our understanding of these complex interactions in different systems, the use of non-specific and one-dimensional assays for anti-oxidant capacity would be risky because they do not provide information on the biological target(s) protected. . .

CONCLUSIONS

. . . When testing antioxidant activity of potential food antioxidants or bioactive compounds, the first aim may be to develop a model system where basic chemical principles can be deduced. On the other hand, the true effectiveness of antioxidants cannot be properly assessed unless the conditions, ie the complexity of the system, are as close as practically possible to the conditions under which protection against autoxidation is required. Targeting of antioxidants to prevent particular free radical formation steps and oxidative deterioration processes requires detailed understanding of the mechanisms of oxidation. Specific lipid model systems should mimic the food or physiological target systems to be protected as close as practically possible. There are various sources and types of oxidation and we should first define the targets of oxidation - lipids, protein, DNA-before selecting methods to assess the protective properties of antioxidants under the conditions of their potential action and use. . . In view of the wide divergence of results of natural antioxidants in foods and biological systems, more valid guidelines and assay protocols are urgently needed to bring some order to the present chaos in this important field. Our understanding of the effects of antioxidant compounds can only be improved if more specific methodology is used capable of defining what products are formed and inhibited by antioxidants depending upon conditions, systems and targets of protection."

Another article (copy enclosed) entitled, "Lipid Oxidation: Mechanisms, Products and Biological Significance" (E. N. Frankel, J. Am. Oil Chem. Soc. Vol. 61, No. 12, 1908-1917, 1984) contains (page 1915) numerous examples of biological damage that can be caused to proteins by free radicals.

In yet another article (copy enclosed) entitled "Chemistry of Free Radical and Singlet Oxidation of Lipids," (E. N. Frankel, Prog. Lipid Res. 23, 197-221, 1985), the same author reviews structural studies of primary and secondary products of lipid oxidation, and states (page 197) that the decomposition products are implicated in many in vivo biological processes. This author points out (page 213) that high molecular weight products of lipid oxidation occur in high yields, and (page 219) that the levels of low molecular weight products are small compared to the "1 to 8%" of "mainly polymeric" substances generated by free radical attack.

The OSI test that is described in the present application measures specifically the low molecular weight breakdown products of oxidation of lipids. In contrast, the test described in the '052 patent measures the prevention of the formation of high molecular products by free radical crosslinking of protein in skin and hair.

Any one of the compounds or compositions that are described in the rejected claims of the application may have additional properties or applications as yet undiscovered. For example, it is well established that natural products having cellular reproductive inhibition in the brine shrimp assay as described in Abbott et al. (Industrial Crops and Products 16, 46-53 (2002)) may also inhibit cancer cells and have therapeutic value. Some of the compounds that have been determined to be most effective in the present application, such as 1,3-di(3-methoxybenzyl) thiourea, were determined to be the least effective in cellular inhibition in the above-cited Abbott et al. publication. The same logic should be applied to the free radical inhibition in hair and skin compared with oxidative stability enhancement.

The subject matter that is described in the rejected claims of the present application is different in both the mechanism of action, and the substrate on which it acts, in comparison with the subject matter that is claimed in the '052 patent. Preventing damage to hair and skin by free radicals is accomplished by reacting with high energy free radicals, specifically reactive oxygen species, as is described in the Background of the Invention section of the '052 patent. Enhancing antioxidative effects in oils with the addition of the compounds and compositions that are described in the rejected claims of the application, in contrast, is accomplished by decomposing hydroperoxy derivatives of the oils, before the oils proceed to the next step to decomposition to aldehydes and acids.

17. All statements in the Declaration of my own knowledge are true and all statements made on information and belief are believed to be true. I am aware that willful false statements and the like are punishable by fine and imprisonment, or both (18 U.S.C. §1001) and may jeopardize the validity of the application or any patent issuing thereon.

Thomas P Abbott

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September 13, 2005

Date

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